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OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION

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MEMORANDUM

SUBJECT: Exposure and Risk Estimate Comparison of Two Fipronil Perimeter Treatments that Vary in Both Application Rate and Area Treated

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The Registration Division (RD) requested a comparison of the exposure estimates (EECs) and risk quotients (RQs) for two fipronil perimeter treatments (Termidor SC and Control Solutions, Inc.) that vary in both application rate and area treated. The Termidor SC (EPA Reg. No. 7969-210) perimeter use has an application rate of 0.3267 lb ai/A (2 applications per year) to a 1 ft perimeter around the building measured up the side of the wall from the soil surface (referred to as "1' up") and a 1 ft perimeter measured horizontally from the wall of the building out across the soil or yard surface ("1' out"). Therefore, the entire Termidor perimeter treatment is referred to as "1' up and 1' out". Control Solutions, Inc. (CSI; EPA Reg. No. 53883-328) perimeter use has an application rate of 0.1838 lb ai/A (also 2 applications per year) to a 2' up and 2' out perimeter treatment area. **This analysis shows the CSI application would apply 14.3% more fipronil over EFED's standard residential scenario watershed than the Termidor application.**

I. Fate Profile for Fipronil

Fipronil dissipation appears to be dependent on photodegradation in water, microbially-mediated degradation, and soil binding. Data indicate that fipronil is relatively persistent and immobile in terrestrial environments. In aquatic environments, a determination of the environmental behavior of fipronil is more tentative because soil and aquatic metabolism studies provide contradictory data on fipronil's persistence to microbially-mediated degradation processes. Photolysis is expected to be a major factor in controlling fipronil dissipation in aquatic environments. Fipronil is highly bioaccumulative in fish (380× in the whole body); however, 99% of these residues were lost from the fish during the 14-day depuration period.

Fipronil degrades to form persistent and immobile degradates [fipronil sulfide (MB 45950), fipronil sulfone (MB 46136), and MB 46513]; these degradates are considered in the HED dietary tolerance expression for fipronil. Given that fipronil and its degradates have a moderate to high sorption affinity to organic carbon, it is likely that sorption to soil organic matter will limit fipronil residue movement into ground and surface waters. However, fipronil and degradate residues may have the potential to move to groundwater in very vulnerable soils (*e.g.*, coarse-textured soils with low organic matter content) and to surface water when bound to particles entrained in runoff from erodible soils.

II. Exposure Estimation

Aquatic Exposure

The Surface Water Concentration Calculator (SWCC) model was used to provide estimated environmental concentrations (EECs) of fipronil and its degradates from use around the perimeters of man-made structures in Louisiana based on a Termidor® 1' up and 1'out (EPA Reg. No. 7969-21 0) and CSI 2' up and 2'out high and low dilutions (EPA Reg. No. 53883-328) and (Tables 1 and 2). The inputs and general modeling methods used to calculate EECs followed those in the RED risk assessment (USEPA (2007) with the following modifications:

- the proposed application rates (0.3267 lb ai/A – Termidor and 0.1838 lb ai/A – CSI high dilution);
- The number of applications (two);
- Application dates of March 1st and September 1st (neither label specifies a minimum re-treatment interval);
- Updated fate data were incorporated (Table 2);
- Louisiana meteorological data was used; and
- A toxic equivalents (TEQ) approach was employed.

The TEQ approach was considered the most appropriate approach because some of fipronil's degradates are more toxic to non-target organisms than the parent fipronil. The TEQ approach allows exposure to the combination of parent and degradates to be expressed in terms of the parent alone by summing the EECs after correcting for each degradate's toxicity relative to the parent's toxicity. Conversion factors for fipronil sulfone (MB6136), MB46513, and fipronil

sulfide (MB45950) were assumed to be 23.9%, 0.96% and 4.9%, of applied parent, respectively (maximum fate study detections).

Table 1. PRZM/EXAMS Input Parameters for Fipronil and Degradates.

Parameter	Fipronil	Fipronil Sulfide	Fipronil Sulfone	MB46513
Soil K_{OC} (g/mL)	727[1] (MRID 44039003)	3911[1] (MRID 44537902)	4208[1] (MRID 44537901)	1290[1] (MRID 44262831)
Aerobic Soil Metabolism $t_{½}$ (days)	218 (MRID 42918663)	700 (Assumed)	700 (Assumed)	660 (MRID 44262830)
Aqueous Photolysis $t_{½}$ (days)	0.33 (MRID 42918661)	Stable (No data)	Stable (No data)	7 (MRID 42918661)
Hydrolysis $t_{½}$ at pH 7	Stable (MRID 42194701)	Stable (No data)	Stable (No data)	Stable (No data)
Aerobic Aquatic Metabolism $t_{½}$ (days)	33.7[2] (MRID 44661301, 44261909)	1400 (2 × ASM $t_{½}$)	1400 (2 × ASM $t_{½}$)	1400 (2 × ASM $t_{½}$)
Anaerobic Aquatic Metabolism $t_{½}$ (days)	160 (MRID 44661301, 44261909)	Stable (MRID 49151519)	Stable (MRID 49151519)	Stable (MRID 49151519)
Water Solubility (mg/L)	2.3 (MRID 47723915)	0.04 (USEPA 2007)	0.16 (MRID 44350001)	0.95 (MRID 44350002)

[1]Mean KOC value.
[2]90th percentile of the observed half-lives.
ASM = Aerobic soil metabolism.

Since the 2007 assessment, USEPA has developed a standard residential exposure scenario using a quarter acre lot and houses with a 1000 ft^2 footprints. Houses are assumed to be square with sides of 31.6 ft and a 15 ft. wide driveway to the house. Therefore, the perimeter of the house that is treated on sod or lawn (pervious surfaces) within 1 or 2 feet of the house foundation is:

$$(31.6\text{ft} \times 2\text{sides} + (31.6\text{ft}+2\text{ft}) \times 2\text{sides} - 15\text{ft driveway}) \times 1\text{ft} = 115.4\text{ft}^2 - \text{Termidor}$$
$$(31.6\text{ft} \times 2\text{sides} + (31.6\text{ft}+4\text{ft}) \times 2\text{sides} - 15\text{ft driveway}) \times 2\text{ft} = 238.8\text{ft}^2 - \text{CSI}$$

Where: 31.6 ft is the length of the house; and 2 ft or 4 ft is twice the perimeter widths to account for the additional corner areas of the perimeter.

There is an additional 1 or 2 ft of the walls of the house that is treated which has the potential to wash-off to this same area of pervious surface:

$$(31.6\text{ft} \times 4\text{sides} - 15\text{ft driveway}) \times 1\text{ft} = 111.4\text{ft}^2 - \text{Termidor}$$
$$(31.6\text{ft} \times 4\text{sides} - 15\text{ft driveway}) \times 2\text{ft} = 222.8\text{ft}^2 - \text{CSI}$$

Therefore the total area of treatment that may drain through pervious area is 226.8 ft^2 (115.4 ft^2 + 111.4 ft^2) for Termidor or 461.6 ft^2 (238.8 ft^2 + 222.8 ft^2) for CSI.

It is assumed that treatment to both horizontal and vertical surfaces (lawn, flower beds, driveway,

walls, and garage door) are available to run off the treated area. In the Termidor exposure scenario, the fraction of the watershed that is treated and expected to drain through pervious surfaces is:

$$226.8\text{ft}^2/\text{house} \times 58\text{houses/watershed} \div 1076391\text{ft}^2/\text{watershed} \times 100 = 1.222\%$$

(Termidor exposure scenario from pervious surfaces)

In the CSI exposure scenario, the fraction of the watershed that is treated and expected to drain through pervious surfaces is:

$$461.6\text{ft}^2/\text{house} \times 58\text{houses/watershed} \div 1076391\text{ft}^2/\text{watershed} \times 100 = 2.487\%$$

(CSI exposure scenario from pervious surfaces)

Additionally under the Termidor exposure scenario, the area of the side of the house that is treated (up 1 ft) and assumed to wash-off to a 15 ft wide driveway that is also treated for 1 ft out (impervious surface) is:

$$1\text{ft} \times 15\text{ft} + 1\text{ft} \times 15\text{ft} = 30\text{ft}^2$$

Therefore:

$$30\text{ft}^2/\text{house} \times 58\text{houses/watershed} \div 1076391\text{ft}^2/\text{watershed} \times 100 = 0.1617\%$$

(Termidor exposure scenario from impervious surfaces)

Similarly under the CSI exposure scenario, the area of the side of the house that is treated (up 2 ft) and assumed to wash-off to a 15 ft wide driveway that is also treated for 2 ft out (impervious surface) is:

$$2\text{ft} \times 15\text{ft} + 2\text{ft} \times 15\text{ft} = 60\text{ft}^2$$

Therefore:

$$60\text{ft}^2/\text{house} \times 58\text{houses/watershed} \div 1076391\text{ft}^2/\text{watershed} \times 100 = 0.3233\%$$

(CSI exposure scenario from impervious surfaces)

The aquatic exposure analysis EECs are somewhat different than typically produced by EFED because of the use pattern involved (residential) and the consideration of a simultaneous exposure to the parent degradates of toxicological concern. The residential exposure scenario requires the SWCC to be run twice – once for pervious surfaces and once for impervious surfaces. The toxic equivalents (TEQ) approach requires PRZM/EXAMS to be run four times for each scenario to produce EECs for fipronil and each of three degradates. The daily time series produced by these multiple model runs are post-processed to produce a high and low residential EECs that are specific for each organism group (freshwater fish, estuarine/marine fish, etc.) that EFED typically assesses (Table 2).

Table 2. Surface Water and Pore Water Fipronil TEQ Estimated Environmental Concentrations (EECs) for Proposed Perimeter Treatments

Proposed Label Use	PRZM/EXAMS Scenario[1]	Application Rate	EC_{50}-Based EEC (µg ai/L)	NOAEC-Based EEC (µg ai/L)
Freshwater Fish (surface water)				
Perimeter spray	Termidor	0.3267 lb ai/A	0.36	0.79
	CSI	0.1838 lb ai/A	0.41	0.90
Estuarine/Marine Fish (surface water)				
Perimeter spray	Termidor	0.3267 lb ai/A	0.59	0.45
	CSI	0.1838 lb ai/A	0.66	0.51
Freshwater Invertebrates (surface water)				
Perimeter spray	Termidor	0.3267 lb ai/A	0.11	0.09
	CSI	0.1838 lb ai/A	0.13	0.10
Estuarine/Marine Invertebrates (surface water)				
Perimeter spray	Termidor	0.3267 lb ai/A	0.33	0.16
	CSI	0.1838 lb ai/A	0.37	0.19
Benthic Invertebrates (pore water)				
Perimeter spray	Termidor	0.3267 lb ai/A	0.20	N/A
	CSI	0.1838 lb ai/A	0.23	N/A
Aquatic Vascular Plants (surface water)				
Perimeter spray	Termidor	0.3267 lb ai/A	0.17	0.17
	CSI	0.1838 lb ai/A	0.19	0.19
Aquatic Non-Vascular Plants (surface water)				
Perimeter spray	Termidor	0.3267 lb ai/A	0.17	0.20
	CSI	0.1838 lb ai/A	0.20	0.23

[1] 100% application efficiency, 0% drift

III. Toxicity Profile for Fipronil

The toxicity of fipronil and three of it degradates to aquatic groups is summarized in Table 3. Only the most sensitive endpoints for each taxa are reported. In some instances, endpoints were estimated (see comments column for explanations).

Table 3. Aquatic Toxicity Profile of the Most Sensitive Endpoints for Parent Fipronil and Degradates Fipronil Sulfide (MB 45950), Fipronil Sulfone (MB 46136), and MB 46513

Assessment Endpoint	Acute/ Chronic	Chemical TGAI/TEP – % ai	Species	Toxicity Value Used in Risk Assessment and Acute Toxicity Classification (If Applicable)	Citation/ MRID Classification	Comments
Freshwater fish (surrogate for aquatic-phase amphibians)	Acute	Fipronil TGAI – 100%	Bluegill sunfish (*Lepomis macrochirus*)	96-hr LC_{50} = 83 µg ai/L Very highly toxic	42918624 Acceptable	96-hr NOAEC = 43 µg ai/L (based on sublethal effects) Sublethal effects: partial/complete loss of equilibrium and lethargy
		Fipronil Sulfide (MB 45950)	NA	Assumed LC_{50} = 83 µg ai/L	NA	Assumed to be equal to the LC_{50} for parent fipronil
		Fipronil Sulfone (MB 46136) TGAI – 99.2%	Bluegill sunfish (*Lepomis macrochirus*)	96-hr LC_{50} = 25 µg ai/L Very highly toxic	42918674 Acceptable	96-hr NOAEC = 6.7 µg ai/L (based on sublethal effects) Sublethal effects: darkened pigmentation, erratic swimming behavior, partial complete loss of equilibrium, surfacing, and lethargy
		MB 46513 TGAI – 98.6%	Bluegill sunfish (*Lepomis macrochirus*)	96-hr LC_{50} = 20 µg ai/L Very highly toxic	43279702 Acceptable	96-hr NOAEC = 9.6 µg ai/L Sublethal effects: anterior extension pectoral fins, lying on the bottom of the test vessel, partial/complete loss of equilibrium, lethargy, and erratic swimming behavior
	Chronic	Fipronil TGAI – 96.7%	Rainbow trout (*Oncorhynchus mykiss*)	Early life stage 90-day NOAEC = 6.6 µg ai/L (based on reduction in larval length)	42918627 Acceptable	90-day LOAEC = 15 µg ai/L
		Fipronil Sulfide (MB 45950)	NA	Assumed NOAEC = 6.6 µg ai/L	NA	Assumed to be equal to the NOAEC for parent fipronil
		Fipronil Sulfone (MB 46136)	NA	Estimated NOAEC = 0.67 µg ai/L	NA	Estimated NOAEC using $ACR_{(rainbow\ trout)}$ for parent fipronil = $\frac{LC_{50(MB\ 46136;\ most\ sensitive\ fish\ species)}}{(LC_{50}:NOAEC_{(fipronil;\ rain\ bow\ trout)})}$ = $\frac{LC_{50(MB\ 46136;\ bluegill\ sunfish)}}{(LC_{50}:NOAEC_{(fipronil;\ rain\ bow\ trout)})}$ = 25 µg ai/L / (246 µg ai/L/6.6 µg ai/L) = 0.67 µg ai/L
		MB 46513	NA	Estimated NOAEC = 0.54 µg ai/L	NA	Estimated NOAEC using $ACR_{(rainbow\ trout)}$ for parent fipronil = $\frac{LC_{50(MB\ 46513;\ most\ sensitive\ fish\ species)}}{(LC_{50}:NOAEC_{(fipronil;\ rain\ bow\ trout)})}$ = $\frac{LC_{50(MB\ 46513;\ bluegill\ sunfish)}}{(LC_{50}:NOAEC_{(fipronil;\ rain\ bow\ trout)})}$

Assessment Endpoint	Acute/ Chronic	Chemical TGAI/TEP – % ai	Species	Toxicity Value Used in Risk Assessment and Acute Toxicity Classification (If Applicable)	Citation/ MRID Classification	Comments
						= 20 µg ai/L / (246 µg ai/L/6.6 µg ai/L) = 0.54 µg ai/L
Freshwater invertebrates	Acute	Fipronil TGAI – >98%	Black fly (*Simulium vittatum*)	LC_{50} = 0.22 µg ai/L Very highly toxic	Overmyer et al., 2005	
		Fipronil Sulfide (MB 45950) TGAI – 100%	Water flea (*Daphnia magna*)	48-hr EC_{50} = 100 µg ai/L Highly toxic	42918669 Acceptable	48-hr NOAEC < 34 µg ai/L (based on mortality) Effects: 0, 5, 10, 15, 60, 70, and 95% immobility in the negative control, solvent control, 34, 60, 100, 180, and 320 µg ai/L treatment groups; lethargy at ≥60 µg ai/L
		Fipronil Sulfone (MB 46136) TGAI – 100%	Water flea (*Daphnia magna*)	48-hr EC_{50} = 29 µg ai/L Very highly toxic	42918671 Acceptable	48-hr NOAEC < 19 µg ai/L (based on mortality and sublethal effects) Effects: 5, 5, 45, 35, 75, 90, and 100% immobility in the negative control, solvent control, 19, 31, 56, 89, and 150 µg ai/L treatment groups; lethargy and resting on the bottom
		MB 46513 TGAI – 97.8%	Water flea (*Ceriodaphnia dubia*)	LC_{50} = 43.8 µg ai/L Highly toxic	Konwick et al., 2005	
	Chronic	Fipronil	NA	Estimated NOAEC = 0.011 µg ai/L	NA	Estimated NOAEC using lowest $LC_{50(fipronil;\ FW\ invert)}$ and $ACR_{(fipronil;\ D.\ magna)}$ = $LC_{50(fipronil;\ black\ fly)}$ / $ACR_{(fipronil;\ D.\ magna)}$ = 0.22 µg ai/L / (190 µg ai/L/9.8 µg ai/L) = 0.011 µg ai/L
		Fipronil Sulfide (MB 45950)	NA	Estimated NOAEC = 0.11 µg ai/L	NA	Estimated NOAEC using lowest $LC_{50\ (MB\ 45950;\ FW\ invert)}$ and $ACR_{(fipronil;\ black\ fly)}$ =$LC_{50(MB\ 45950;\ D.\ magna)}$ / $ACR_{(fipronil;\ D.\ magna)}$ =2.13 µg ai/L / (0.22 µg ai/L/0.011 µg ai/L) =0.11 µg ai/L
		Fipronil Sulfone (MB 46136)	NA	Estimated NOAEC = 0.037 µg ai/L	NA	Estimated NOAEC using lowest $LC_{50(MB\ 46136;\ FW\ invert)}$ and $ACR_{(fipronil;\ black\ fly)}$ =$LC_{50(MB\ 46136;\ D.\ magna)}$ / $ACR_{(fipronil;\ D.\ magna)}$ =0.72 µg ai/L / (0.22 µg ai/L/0.011 µg ai/L) =0.037 µg ai/L

Assessment Endpoint	Acute/ Chronic	Chemical TGAI/TEP – % ai	Species	Toxicity Value Used in Risk Assessment and Acute Toxicity Classification (If Applicable)	Citation/ MRID Classification	Comments
		MB 46513 TGAI – 97.81%	Water flea (*Daphnia magna*)	21-day NOAEC = 41 µg ai/L (based on reduction in length and weight)	43279704 and 44812801 Acceptable	21-day NOAEC = 100 µg ai/L Other effects: reduction in survival a 260 µg ai/L
Estuarine/ marine fish	Acute	Fipronil TGAI – 96.1%	Sheepshead minnow (*Cyprinodon variegatus*)	96-hr LC_{50} = 130 µg ai/L Highly toxic	43291702 Acceptable	96-hr NOAEC < 110 µg ai/L (based on sublethal effects) Sublethal effects: erratic swimming behavior, partial/complete loss of equilibrium
		Fipronil Sulfide (MB 45950)	NA	Estimated LC_{50} = 130 µg ai/L	NA	Assumed to be equal to the LC_{50} for parent fipronil
		Fipronil Sulfone (MB 46136)	NA	Estimated LC_{50} = 21 µg ai/L	NA	Estimated LC_{50} using $LC_{50(\text{fipronil; sheepshead minnow})}$ and largest $LC_{50(\text{fipronil; FW fish})}$:$LC_{50(\text{MB46136; FW fish})}$ = $LC_{50(\text{fipronil; sheepshead minnow})}$ / $LC_{50(\text{fipronil; rainbow trout})}$:$LC_{50(\text{MB46136; rainbow trout})}$ = 130 µg ai/L / (246 µg ai/L/39 µg ai/L) = 21 µg ai/L
		MB 46513	NA	Estimated LC_{50} = 31 µg ai/L	NA	Estimated LC_{50} using $LC_{50(\text{fipronil; sheepshead minnow})}$ and largest $LC_{50(\text{fipronil; FW fish})}$:$LC_{50(\text{MB 46513; FW fish})}$ = $LC_{50(\text{fipronil; sheepshead minnow})}$ / $LC_{50(\text{fipronil; bluegill sunfish})}$:$LC_{50(\text{MB 46513; bluegill sunfish})}$ = 130 µg ai/L / (83 µg ai/L/20 µg ai/L) = 31 µg ai/L
	Chronic	Fipronil TGAI – 97.08% Radiolabeled – 99.4%	Sheepshead minnow (*Cyprinodon variegatus*)	NOAEC = 0.24 µg ai/L (based on reduction in length and weight)	446085502 Acceptable	LOAEC = 0.41 µg ai/L Other effects: reduction in egg hatching at 2.9 µg ai/L
		Fipronil Sulfide (MB 45950)	NA	Assumed NOAEC = 0.24 µg ai/L	NA	Assumed to be equal to the NOAEC for parent fipronil
		Fipronil Sulfone (MB 46136)	NA	Estimated NOAEC = 0.039 µg ai/L	NA	Estimated NOAEC using Estimated $LC_{50(\text{MB 46136; E/M fish})}$ and $ACR_{(\text{fipronil; sheepshead minnow})}$ = 21 µg ai/L / (130 µg ai/L/0.24 µg ai/L) = 0.039 µg ai/L
		MB 46513	NA	Estimated NOAEC = 0.057 µg ai/L	NA	Estimated NOAEC using Estimated $LC_{50(\text{MB 46513; E/M fish})}$ and $ACR_{(\text{fipronil; sheepshead minnow})}$ = 31 µg ai/L / (130 µg ai/L/0.24 µg ai/L) = 0.057 µg ai/L

Assessment Endpoint	Acute/ Chronic	Chemical TGAI/TEP – % ai	Species	Toxicity Value Used in Risk Assessment and Acute Toxicity Classification (If Applicable)	Citation/ MRID Classification	Comments
Freshwater sediment dwelling invertebrates	Acute	Fipronil TGAI – 98.3%	Midge (*Chironomus tentans*)	Sediment exposure <u>Sediment</u> 10-day NOAEC = 16 µg ai/kg-sediment <u>Pore water</u> 10-day NOAEC = 0.24 µg ai/L <u>Overlying water</u> 10-day NOAEC = < 0.056 µg ai/L (based on mortality)	45878001 Acceptable	<u>Sediment</u> 10-day LC_{50} = 30.7 µg ai/kg-sediment <u>Pore water</u> 10-day LC_{50} = 0.41 µg ai/L raw data not submitted for weight; study author-reported endpoint for growth (weight): 10-day EC_{50} = 50 µg ai/kg-sediment
		Fipronil Sulfide (MB 45950) TGAI – 99.5%	Midge (*Chironomus tentans*)	Sediment exposure <u>Sediment</u> 10-day NOAEC = 29 µg ai/kg-sediment <u>Pore water</u> 10-day NOAEC = 0.35 µg ai/L <u>Overlying water</u> 10-day NOAEC = 0.013 µg ai/L (based on mortality)	45084801 Acceptable	<u>Sediment</u> 10-day NOAEL = 54 µg ai/kg-sediment (based on growth) 10-day EC_{50} = 50.9 µg ai/kg-sediment (based on growth) 10-day LC_{50} = 116.9 µg ai/kg-sediment <u>Pore water</u> 10-day NOAEL = 0.94 µg ai/L (based on growth) 10-day EC_{50} = 0.66 µg ai/L (based on growth) 10-day LC_{50} = 2.13 µg ai/L <u>Overlying water</u> 10-day NOAEL = 0.022 µg ai/L (based on growth)
		Fipronil Sulfone (MB 46136)	Midge (*Chironomus tentans*)	Sediment exposure <u>Sediment</u>	45175901 Acceptable	<u>Sediment</u> 10-day EC_{50} = 34.8 µg ai/kg-sediment (based on growth)

Assessment Endpoint	Acute/ Chronic	Chemical TGAI/TEP – % ai	Species	Toxicity Value Used in Risk Assessment and Acute Toxicity Classification (If Applicable)	Citation/ MRID Classification	Comments
		TGAI – 99.01%		10-day NOAEC = 9.1 µg ai/kg-sediment <u>Pore water</u> 10-day NOAEC = 0.073 µg ai/L <u>Overlying water</u> 10-day NOAEC = 0.0052 µg ai/L (based on growth)		10-day NOAEL = 14 µg ai/kg-sediment (based on mortality) 10-day LC_{50} = 44.8 µg ai/kg-sediment <u>Pore water</u> 10-day EC_{50} = 0.41 µg ai/L (based on growth) 10-day NOAEL = 0.30 µg ai/L (based on mortality) 10-day LC_{50} = 0.72 µg ai/L <u>Overlying water</u> 10-day NOAEL = 0.0069 µg ai/L (based on mortality)
		MB 46513 TGAI – 97.8% Radiolabeled – 99.1-99.6%	Midge (*Chironomus tentans*)	Sediment exposure <u>Sediment</u> 10-day NOAEC = < 185 µg ai/kg-sediment (based on growth)	45375901 Supplemental (due to unreliable pore water concentrations)	<u>Sediment</u> 10-day EC_{50} = 520 µg ai/kg-sediment (based on growth) 10-day NOAEL = 185 µg ai/kg-sediment (based on mortality) 10-day LC_{50} = 1300 µg ai/kg-sediment
	Chronic	MB 45950 Radiolabeled – 99.5%	Midge (*Chironomus riparius*)	<u>Sediment</u> 28-day NOAEC = 1.85 µg TTR/kg-dw sediment <u>Overlying water</u> 28-day NOAEC = 0.015 µg TTR/L (based on emergence and development rates)	45851001 Supplemental (non-guideline)	NOAEC = 1.1* µg/kg-dw sediment (day -10 conc.) (based on lethargy) *may be an overestimated NOAEC as the concentration was not measured on days 0 and 28 at this treatment level

Assessment Endpoint	Acute/ Chronic	Chemical TGAI/TEP – % ai	Species	Toxicity Value Used in Risk Assessment and Acute Toxicity Classification (If Applicable)	Citation/ MRID Classification	Comments
Estuarine/ marine invertebrates	Acute	Fipronil TGAI – 96.1%	Mysid shrimp (*Americamysis bahia*)	96-hr LC_{50} = 0.140 µg ai/L Very highly toxic	43279701 Acceptable	96-hr NOAEC < 62 µg ai/L
		Fipronil Sulfide (MB 45950) TGAI – 99.7%	Mysid shrimp (*Americamysis bahia*)	96-hr LC_{50} = 0.077 µg ai/L Very highly toxic	45156302 Acceptable	96-hr NOAEC = 33 µg ai/L Sublethal effects: None
		Fipronil Sulfone (MB 46136) TGAI – 99.7%	Mysid shrimp (*Americamysis bahia*)	96-hr LC_{50} = 0.056 µg ai/L Very highly toxic	45165301 Acceptable	96-hr NOAEC = 0.031 µg ai/L Sublethal effects: None
		MB 46513 TGAI – 97.8%	Mysid shrimp (*Americamysis bahia*)	96-hr LC_{50} = 1.5 µg ai/L Very highly toxic	45120001 Acceptable	96-hr NOAEC = 0.66 µg ai/L
		Fipronil TGAI – 96.1%	Eastern oyster (*Crassostrea virginica*)	96-hr EC_{50} = 770 µg ai/L Highly toxic	43291701 Acceptable	Sublethal effects: reduced fecal and pseudofecal production at 1.2 µg ai/L
	Chronic	Fipronil TGAI – 97.7%	Mysid shrimp (*Americamysis bahia*)	28-day NOAEC < 0.005 µg ai/L (based on reduction in male weight)	43681201 Supplemental (due to lack of a NOAEC)	28-day LOAEC = <0.005 µg ai/L Other effects: reduction in male length at ≥15 µg ai/L; reduction in female weight and length at 57 and ≥28 µg ai/L, respectively; reduction in reproduction and F1 survival at 57 µg ai/L
		Fipronil Sulfide (MB 45950) TGAI – 99.5%	Mysid shrimp (*Americamysis bahia*)	28-day NOAEC = 0.0046 µg ai/L (based on reduction in male weight)	45259202 Supplemental (due to the lack of a solvent control)	28-day LOAEC = 0.0087 µg ai/L Other effects: reduction in reproduction, F1 survival, male length and female weight at 35 µg ai/L
		Fipronil Sulfone (MB 46136) TGAI – 99%	Mysid shrimp (*Americamysis bahia*)	28-day NOAEC < 0.0026 µg ai/L (based on reduction in female weight)	45259203 Supplemental (due to the lack of a NOAEC and solvent control)	28-day LOAEC = 0.0026 µg ai/L Other effects: reduction in male weight at ≥9.3 µg ai/L; reduction in reproduction and male length at ≥19 µg ai/L
		MB 46513	NA	Estimated NOAEC = 0.054 µg ai/L	NA	Estimated NOAEC using lowest $LC_{50(MB\ 46513;\ SW\ invert)}$ and $ACR_{(fipronil;\ A.\ bahia)}$

Assessment Endpoint	Acute/ Chronic	Chemical TGAI/TEP – % ai	Species	Toxicity Value Used in Risk Assessment and Acute Toxicity Classification (If Applicable)	Citation/ MRID Classification	Comments
						= $LC_{50(MB\ 46513;\ A.\ bahia)}$ / $ACR_{(fipronil;\ A.\ bahia)}$ = 1.5µg ai/L / (0.140 µg ai/L/0.005µg ai/L) = 0.054µg ai/L
Aquatic plants	Vascular	Fipronil TGAI – 96.1%	Duckweed (*Lemna gibba*)	14-day EC_{50} > 100 µg ai/L 14-day NOAEC = 100 µg ai/L (based on number of fronds and dry weight)	42918656 Acceptable	
		Fipronil Sulfide (MB 45950)	NA	Assumed EC_{50} > 100 µg ai/L Assumed NOAEC = 100 µg ai/L	NA	Assumed to be equal to the EC_{50} and NOAEC for parent fipronil
		Fipronil Sulfone (MB 46136)	NA	Assumed EC_{50} > 100 µg ai/L Assumed NOAEC = 100 µg ai/L	NA	Assumed to be equal to the EC_{50} and NOAEC for parent fipronil
		MB 46513	NA	Assumed EC_{50} > 100 µg ai/L Assumed NOAEC = 100 µg ai/L	NA	Assumed to be equal to the EC_{50} and NOAEC for parent fipronil
	Non-vascular	Fipronil TGAI – 96.1%	Freshwater diatom (*Navicula pelliculosa*)	5-day EC_{50} > 120 µg ai/L 5-day NOAEC = 120 µg ai/L (based on cell density)	42918658 Acceptable	
		Fipronil Sulfide (MB 45950)	NA	Assumed EC_{50} > 120 µg ai/L Assumed NOAEC = 120 µg ai/L	NA	Assumed to be equal to the EC_{50} and NOAEC for parent fipronil
		Fipronil Sulfone (MB 46136)	NA	Assumed EC_{50} > 120 µg ai/L Assumed NOAEC = 120 µg ai/L	NA	Assumed to be equal to the EC_{50} and NOAEC for parent fipronil
		MB 46513 TGAI – 98.6%	Green alga (*Selenastrum capricornutum*)	5-day EC_{50} = 76 µg ai/L 5-day EC_{05} = 7.5 µg ai/L (based on cell density)	43279705 Acceptable	Effects: Statistically-significant reductions in cell density at all concentrations tested; 5-day NOAEC < 12 µg ai/L

The toxicity of fipronil and degradates MB 45950 and MB 46136 to terrestrial taxa are reported in Table 4. Quantitative data for honeybees were not available; however, some qualitative data were available from the open literature. Mayer and Lunden (1999) (ECOTOX #62630) determined contact 24-hr LD_{50}s for three species of bees: alkali bee (*Nomia melanderi*), honeybee (*Apis mellifera*), and alfalfa leafcutter bee (*Megachile rotundata*). The corresponding LD_{50}s were 1.130 µg ai/bee for the alkali bee, 0.013 µg ai/bee for the honeybee, and 0.004 µg ai/bee for the alfalfa leafcutter bee. A second study, Oliveira Jacob *et al.* (2013), calculated a contact (24-hr LD_{50} = 0.54 ng ai/bee) and dietary (24-hr LC_{50} = 0.24 ng ai/µL-diet) toxicity endpoint for the stingless bee (*Scaptotrigona postica*). Neither study used a negative control, although both studies had solvent (acetone) controls. Mortality data for the solvent control was not reported; thus these studies can only be used qualitatively to characterize the toxicity of fipronil to terrestrial invertebrates.

Table 4. Terrestrial Toxicity Profile for Parent Fipronil and Degradates Fipronil Sulfide (MB 45950), Fipronil Sulfone (MB 46136), and MB 46513

Assessment Endpoint	Acute/ Chronic	Chemical TGAI/TEP – % ai	Species	Toxicity Value Used in Risk Assessment and Acute Toxicity Classification (If Applicable)	Citation or MRID # Classification	Comment
Birds (surrogate for terrestrial-phase amphibians and reptiles)	Acute single oral dose	Fipronil TGAI – 96%	Bobwhite quail (*Colinus virginianus*)	21-day LD_{50} = 11.3 mg ai/kg-bw Highly toxic	42918617 Acceptable	21-day NOAEL < 1 mg ai/kg-bw (based on reduction in food consumption during the first 3 days) Sublethal effects: at ≥4.64 mg ai/kg-bw, lethargy, moving the head from side to side when disturbed, chalky diarrhea, anorexia, stumbling, ataxia, tremors, tachypnea, wing-beat convulsions, tetany, spasms, loss of balance, piloerection, sitting, failure to respond to external stimuli, gasping for breath, noticeable weight loss, the appearance of weakness or listlessness, and death; remission achieved by day 18; reduction in body weight at 4.46 and 10 mg ai/kg-bw on days 3, 7, and 14; reductions in body weight before death at 21.5 and 46.4 mg ai/kg-bw; dose-dependent reduction in food consumption during the first 3 days of the test for all treatment groups; reduction in food consumption continued through day 7 at 4.64 mg ai/kg-bw and through day 14 at 10 and 21.5 mg ai/kg-bw
		Fipronil Sulfide (MB 45950)	NA	Estimated LD_{50} = 26.8 mg ai/kg-bw	NA	Estimated LD_{50} using $Acute_{(oral)}$-to-$Acute_{(dietary)}$ Ratio = LD_{50}:$LC_{50(\text{most sensitive avian species})}$*$LC_{50(\text{MB 45960})}$ = LD_{50}:$LC_{50(\text{bobwhite quail})}$*$LC_{50(\text{MB 45960})}$ = (11.3 mg a.i./kg-bw/48 mg ai/kg-diet)*114 mg ai/kg-diet = 26.8 mg ai/kg-bw
		Fipronil Sulfone (MB 46136)	NA	Estimated LD_{50} = 19.7 mg ai/kg-bw	NA	Estimated LD_{50} using $Acute_{(oral)}$-to-$Acute_{(dietary)}$ Ratio = LD_{50}:$LC_{50(\text{most sensitive avian species})}$*$LC_{50(\text{MB 45960})}$ = LD_{50}:$LC_{50(\text{bobwhite quail})}$*$LC_{50(\text{MB 43136})}$ = (11.3 mg ai/kg-bw/48 mg ai/kg-diet)*84 mg ai/kg-diet = 19.7 mg ai/kg-bw
		MB 46513 TGAI – 98.6%	Bobwhite quail (*Colinus virginianus*)	21-day LD_{50} = 5 mg ai/kg-bw Highly toxic	43776601 Acceptable	21-day NOAEL = 3.16 mg ai/kg-bw (based on a reduction in body weight) Sublethal effects: reduction in feed consumption at ≥ 3.16 mg a.i./kg-bw; reduction in body weight on day 7 at ≥14.7 mg a.i./kg-bw

Assessment Endpoint	Acute/ Chronic	Chemical TGAI/TEP – % ai	Species	Toxicity Value Used in Risk Assessment and Acute Toxicity Classification (If Applicable)	Citation or MRID # Classification	Comment
	Sub-acute dietary	Fipronil TGAI – >95%	Bobwhite quail (*Colinus virginianus*)	21-day* = 48 mg ai/kg-diet *5-day exposure; 17-day post-exposure observation Very highly toxic	42918620 Acceptable	21-day NOAEC = 19 mg ai/kg-diet (based on mortality and sublethal effects) Sublethal effects: lethargy, white-colored diarrhea, and anorexia at ≥39 mg ai/kg-diet (remission of survivors at 39 mg ai/kg-diet by end of day 6); reduction in body weight on day 22 at 39 mg ai/kg-diet
		Fipronil Sulfide (MB 45950) TGAI – 98.8%	Bobwhite quail (*Colinus virginianus*)	8-day LC_{50} = 114 mg ai/kg-diet Highly toxic	44890302 Acceptable	8-day NOAEC = 17.8 mg ai/kg-diet (based on sublethal effects) Effects: 0, 0, 10, 0, 0, 30, 100% mortality in the control, 10.0, 17.8, 31.6, 56.2, 100 and 178 mg ai/kg-diet treatment groups; ruffled appearance, wing droop, lethargy, depression, reduced reaction to external stimuli, convulsion, shallow and rapid respiration, and loss of coordination at ≥31.6 mg ai/kg-diet; dose-dependent reduction in body weight gain at 56.2 and 100 mg ai/kg-diet; treatment-related reduction in food consumption at ≥100 mg ai/kg-diet
		Fipronil Sulfone (MB 46136) TGAI – 99.7%	Bobwhite quail (*Colinus virginianus*)	8-day LC_{50} = 84 mg ai/kg-diet Highly toxic	44890301 Acceptable	8-day NOAEC = 17.8 mg ai/kg-diet (based on sublethal effects) Sublethal effects: ruffled appearance, wing droop, lethargy, convulsions, reduced reaction to external stimuli, lower limb weakness, loss of coordination and protracted posture at ≥ 31.6 mg ai/kg-diet; dose-dependent reduction in body weight gain at 56.2 mg ai/kg-diet and weigh loss at ≥100 mg ai/kg-diet
		MB 46513 TGAI – 97.8	Bobwhite quail (*Colinus virginianus*)	8-day LC_{50} = 119.2 mg ai/kg-diet Highly toxic	45259201 Acceptable	8-day NOAEC < 18.6 mg ai/kg-diet (based on sublethal effect of body weight gain between days 0 and 5) Sublethal effects: dose-dependent reduction in body weight gain or loss from days 0 to 5 at treatment levels where total mortality did not occur (*i.e.*, 18.6-49.3 mg ai/kg-diet); reduction in feed consumption from days 0 to 5 at 126 mg ai/kg-diet; ruffled appearance, lethargy, wing droop, loss of coordination, tremors, reduced response to stimuli at ≥49.3 mg ai/kg-diet
	Chronic	Fipronil TGAI – 96.7%	Bobwhite quail (*Colinus virginianus*)	142-day NOAEC = 10 mg ai/kg-diet (no treatment-related effects)	42918622 Supplemental (due to no effects	142-day LOAEC > 10 mg ai/kg-diet Effects: statistically-significant increases in cracked eggs and

Assessment Endpoint	Acute/ Chronic	Chemical TGAI/TEP – % ai	Species	Toxicity Value Used in Risk Assessment and Acute Toxicity Classification (If Applicable)	Citation or MRID # Classification	Comment
					at concentrations tested)	decreases in male body weight at 0.2 and 2 mg ai/kg-diet were not considered treatment-related because there was no effect at 10 mg ai/kg-diet
		Fipronil Sulfide (MB 45950)	NA	Assumed NOAEC = 10 mg ai/kg-diet	NA	Assumed to be equal to the NOAEC for parent fipronil
		Fipronil Sulfone (MB 46136)	NA	Assumed NOAEC = 10 mg ai/kg-diet	NA	Assumed to be equal to the NOAEC for parent fipronil
		MB 46513	NA	Assumed NOAEC = 10 mg ai/kg-diet	NA	Assumed to be equal to the NOAEC for parent fipronil
Mammals	Acute single oral dose	Fipronil TGAI – 93%	Rat	Combined sexes 15-day LD_{50} = 97 mg ai/kg-bw Males 15-day LD_{50} = 92 mg ai/kg-bw Females 15-day LD_{50} = 103 mg ai/kg-bw Moderately toxic	42918628	Sublethal effects: pilo-erection, diarrhea, abnormal body carriage (hunched posture), and abnormal gait (waddling) at ≥50 mg/kg-bw; lethargy at ≥80 mg/kg-bw; decreased respiratory rate in1 male at 80 mg/kg-bw and all individuals at 200 mg/kg-bw; ptosis, pallor of extremities, clonic convulsions, and prostrate stature at 200 mg ai/kg-bw; low body weight gain on day 8 for up to 2 females at each treatment level and for all males surviving treatment; with the exception of one female at 50 mg/kg which showed a slightly low body weight gain, all survivors achieved anticipated body weight gains by study termination
		Fipronil Sulfide (MB 45950)	Rat	LD_{50} = 83 mg ai/kg-bw Moderately toxic	HED memo[a]	
		Fipronil Sulfone (MB 46136) TGAI – 98%	Rat	LD_{50} = 218 mg/kg-bw Moderately toxic	42918675	
		MB 46513	Rat	LD_{50} = 16 mg ai/kg-bw Highly toxic	43235402	
	Chronic	Fipronil	Rat	Reproductive NOAEL = 2.5 mg ai/kg-bw/day NOAEC = 30 mg ai/kg-diet (based on clinical signs, decreased litter size, decreased body weight, decreased mating, decreased fertility index,	42918647	Parental/Systemic NOAEL = 0.25 mg ai/kg-bw/day LOAEL = 2.5 mg ai/kg-bw/day (based on: male/female increased thyroid and liver weights, and female decreased pituitary weight and increased follicular epithelial hypertrophy)

Assessment Endpoint	Acute/ Chronic	Chemical TGAI/TEP – % ai	Species	Toxicity Value Used in Risk Assessment and Acute Toxicity Classification (If Applicable)	Citation or MRID # Classification	Comment
				decreased post-implant survival and offspring postnatal survival, and delayed physical development)		<u>Reproductive</u> LOAEL = 26 mg ai/kg-bw/day <u>Offspring</u> NOAEL = 26 mg ai/kg-bw/day LOAEL = >26 mg ai/kg-bw/day
		Fipronil Sulfide (MB 45950)	NA	NOAEL = 2.5 mg ai/kg-bw/day NOAEC = 30 mg ai/kg-diet	NA	Assumed to be equal to the NOAEC for parent fipronil
		Fipronil Sulfone (MB 46136)	NA	NOAEL = 2.5 mg ai/kg-bw/day NOAEC = 30 mg ai/kg-diet	NA	Assumed to be equal to the NOAEC for parent fipronil
		MB 46513	NA	NOAEL = 2.5 mg ai/kg-bw/day NOAEC = 30 mg ai/kg-diet	NA	Assumed to be equal to the NOAEC for parent fipronil
Terrestrial plants	Seedling emergence	Fipronil TGAI – 80.3%	Oat (*Avena sativa*) Oilseed rape (*Brassica napus*)	<u>Monocot (oat)</u> EC25: 3.49 mg a.i./kg-dry soil (7.1 lb ai/A) EC05: 0.00563 mg a.i./kg-dry soil (0.011 lb ai/A) NOEC: <0.125 mg a.i./kg-dry soil Based on wet weight <u>Dicot (oilseed rape)</u> EC25: 2.27 mg a.i./kg-dry soil (4.62 lb ai/A) NOEC: 0.5 mg a.i./kg-dry soil (1.02 lb ai/A) Based on wet weight	48599701 Supplemental (subset of required species were tested and monocot NOAEC not established)	

[a] Fipronil - Review of toxicity studies (28-day studies with fipronil and metabolite RPA 200766, a developmental neurotoxicity study with fipronil and a paper on the toxicological significance of fipronil and its metabolites). From V.A. Dobozy (Registration Branch 1/HED) to M. Johnson (RD), 8/6/1997

IV. Risk Estimation

Risk to Aquatic Taxa

The following risks to aquatic taxa are identified for both the Termidor and CSI perimeter treatment scenarios. Acute non-listed species LOCs (0.5) were exceeded for all aquatic invertebrates (freshwater, benthic, and estuarine/marine). Chronic RQs exceeded the listed and non-listed species LOC (1) for estuarine/marine fish and freshwater invertebrates. Chronic risk quotients could not be calculated for estuarine/marine invertebrates because the toxicity data were non-definitive. In lieu of this, the toxicity value (<0.005 µg ai/L) was compared directly with the NOAEC-based EECs for estuarine/marine invertebrates (0.17 and 0.19 µg ai/L). Given that the EECs are higher than 0.005 µg ai/L, risk concerns are likely for estuarine/marine invertebrates. Likewise, definitive data were not available for non-listed aquatic vascular plants (>100 µg ai/L) and non-listed non-vascular aquatic plants (>120 µg ai/L). When compared directly with the EECs (vascular aquatic: 0.18 to 0.20 µg ai/L; non-vascular aquatic: 0.21 to 0.24 µg ai/L); the EECs are several order of magnitude lower than the toxicity values. Consequently, risk concerns for aquatic vascular and non-vascular plants are not expected. For benthic invertebrates, chronic toxicity data were not available. Given that chronic risk concerns were identified for both freshwater and estuarine/marine invertebrates, chronic risk is assumed for benthic invertebrates as well.

In summary, risk concerns were identified for estuarine/marine fish (chronic only), freshwater invertebrates, estuarine/marine invertebrates, and benthic invertebrates. Risk concerns were not identified for freshwater fish, estuarine/marine fish (acute only), vascular aquatic plants, and non-vascular aquatic plants (Table 5 and 6).

Table 5. Acute and Chronic Risk Quotients for Aquatic Taxa (Excluding Plants)

Scenario	EC_{50} or LC_{50} (µg ai/L)	NOAEC (µg ai/L)	EC_{50} or LC_{50}-based EEC (µg ai/L)	NOAEC-based EEC (µg ai/L)	Acute RQ	Chronic RQ
Freshwater fish (surface water)						
Termidor	83	6.6	0.36	0.79	0.004	0.12
CSI	83	6.6	0.41	0.90	0.005	0.14
Estuarine/marine fish (surface water)						
Termidor	130	0.24	0.59	0.45	0.005	**1.88*** **
CSI	130	0.24	0.66	0.51	0.005	**2.13*** **
Freshwater invertebrates (surface water)						
Termidor	0.22	0.011	0.11	0.09	**0.50** **	**8.18*** **
CSI	0.22	0.011	0.13	0.10	**0.59** **	**9.09*** **
Estuarine/marine invertebrates (surface water)						
Termidor	0.140	<0.005	0.33	0.16	**2.36** **	ND
CSI	0.140	<0.005	0.37	0.19	**2.64** **	ND

Scenario	EC_{50} or LC_{50} (µg ai/L)	NOAEC (µg ai/L)	EC_{50} or LC_{50}-based EEC (µg ai/L)	NOAEC-based EEC (µg ai/L)	Acute RQ	Chronic RQ
Freshwater benthic organisms (pore water)						
Termidor	0.24	N/A	0.20	N/A	**0.83****	N/A
CSI	0.24	N/A	0.23	N/A	**0.96****	N/A

N/A – chronic toxicity data were not available for EEC calculation and RQ derivation
ND – data were non-definitive and a RQ could not be calculated
* Exceeds acute listed species LOC (0.05)
** Exceeds acute non-listed species LOC (0.5)
*** Exceeds chronic LOC (1.0)

Table 6. Acute and Chronic Risk Quotients for Aquatic Plants

Scenario	EC_{50} or LC_{50} (µg ai/L)	NOAEC (µg ai/L)	EC_{50} or LC_{50}-based EEC (µg ai/L)	NOAEC-based EEC (µg ai/L)	Listed Species RQ	Non-Listed Species RQ
Vascular aquatic plants (surface water)						
Termidor	>100	100	0.17	0.17	ND	0.002
CSI	>100	100	0.19	0.19	ND	0.002
Non-vascular plants (surface water)						
Termidor	>120	120	0.17	0.20	ND	0.002
CSI	>120	120	0.20	0.23	ND	0.002

ND – data were non-definitive and a RQ could not be calculated

V. Conclusions

The CSI application rate (0.1838 lb ai/A) is approximately 56.3% of the Termidor application rate (0.3267 lb ai/A). If the CSI application area (2' up by 2' out) was exactly twice the Termidor application area (1' up by 1' out), the CSI application would apply 12.5% more fipronil around each structure. Because a 2' up by 2' out treatment area is slightly larger than twice the 1' up by 1' out due to additional corner area in the 2' out portion of the perimeter treatment, the CSI treatment area is 203.1% of the Termidor treatment area. Therefore, the CSI application would apply 14.3% more fipronil over EFED's standard residential scenario watershed than the Termidor application.